

Session 1

Biosketches

EPA Co-Chair:

Ravi Subramaniam

EPA NCEA

External Co-Chair:

Melvin Ernest Andersen, PhD, DABT, CIH, FATS

The Hamner Institutes for Health Sciences

Dr. Andersen, the Chief Science Officer, at The Hamner Institutes for Health Sciences in Research Triangle Park, NC, was Professor of Environmental Health at Colorado State (1999 – 2002) and Vice-President of the K.S. Crump Group of ICF Kaiser International Consulting (1994-1998). Between 1971 and 1994, he held positions in toxicology research and research management in the federal government (DoD and US EPA) and in private industry (Chemical Industry Institute of Toxicology). His career contributions include developing biologically realistic models of the uptake, distribution, metabolism, and biological effects of drugs and toxic chemicals and applying these models in safety assessments and quantitative health risk assessments. He has published on dose-dependent genomic responses in rat nasal epithelium following formaldehyde exposure and done kinetic modeling accounting for both inhaled and endogenous formaldehyde in these tissues. Dr. Andersen is author or co-author of 350 papers, 60 book chapters and numerous reports and abstracts. In June 2002, Dr. Andersen received recognition as a highly cited scientist by the Institute for Scientific Information. Dr. Andersen is board certified in industrial hygiene and in toxicology and a Fellow of the Academy of Toxicological Sciences. His current research focuses on developing case studies to show the 21st century vision for toxicity testing in practice with specific cellular signaling pathways. He did a BSc degree in Chemistry at Brown University and a PhD in Biochemistry and Molecular Biology at Cornell University.

Speakers:

Dean Appling

University of Texas at Austin

Dean Appling is the Lester J. Reed Professor of Biochemistry at The University of Texas at Austin, where he has taught and done research for the past 29 years. Dr. Appling earned his B.S. in Biology from Texas A&M University, and his Ph.D. in Biochemistry from Vanderbilt University. The Appling laboratory studies the organization and regulation of metabolic pathways in eukaryotes, focusing on folate-mediated one-carbon metabolism. The lab is particularly interested in understanding how one-carbon metabolism is organized in mitochondria, as these organelles are central players in many human diseases. The laboratory has expertise in mitochondrial isolation and subfractionation, from both cultured cells and from mammalian tissues, and in protein purification and enzyme characterization. More recently, the Appling laboratory has incorporated conditional knockout mouse technologies and metabolic labeling methods with stable isotopes to investigate the roles of mitochondrial one-carbon metabolism in vivo.

James Swenberg

University of North Carolina

[HYPERLINK "<http://www.med.unc.edu/toxicology/about-us/member-profiles/swenberg>"]

Lisa Peterson

University of Minnesota

[HYPERLINK "<http://www.pharmacy.umn.edu/medchem/directory/faculty/peterson/index.htm>"]

Discussants:**Paul Schlosser**

EPA NCEA

[HYPERLINK "http://www.epa.gov/iris/irisworkshops/mltw/wrk_speakers.htm"]

Jeff Ross

EPA

[SEQ CHAPTER \h \r 1]Jeffrey Ross received his Ph.D. in Molecular Biology in 1982 from the University of Texas at Dallas. After completing postdoctoral research at the University of Texas System Cancer Center, he joined the U.S. Environmental Protection Agency as a Research Biologist in 1986. For over 30 years his research has focused on the formation and biological consequences of DNA damage induced by a variety of environmental carcinogens. He currently serves as the Chief of the Carcinogenesis Branch in the Integrated Systems Toxicology Division in the National Health and Environmental Effects Research Laboratory of the US Environmental Protection Agency.

Martyn Smith

University of California, Berkeley

[HYPERLINK "<http://ehs.sph.berkeley.edu/people/smithm.htm>"]

Abstracts

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Speakers:

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Discussants:

Paul Schlosser

EPA NCEA

Jeff Ross

EPA

Martyn Smith

University of California, Berkeley

Case Study Discussant:

Thomas Starr

TBS Associates

Kenny Crump

Independent Consultant

A “bottom-up” linear approach has been proposed for bounding low-dose cancer risks that relies only on the background risk and the background (endogenous) exposure for calculating the linear dose response slope at low doses (Starr and Swenberg 2013). The approach is presented as being conservative, in part because it assumes a linear dose response at endogenous doses. However, this assumption is not conservative as it will underestimate the risk if the dose response to endogenous exposures is sub-linear, which usually seems plausible. Likewise, the statistical upper bound provided for the bottom-up approach is not a valid upper bound on the true low dose slope. Unfortunately, there appears to be no simple way to correct this flaw.

Starr TB and Swenberg JA (2013) A novel bottom-up approach to bounding low-dose human cancer risks from chemical exposures. *Regulatory Toxicology and Pharmacology* 65 (3): 311–315.